REMARKS

Favorable reconsideration of this application as presently amended is respectfully requested. Claims 2-35 are pending and claims 2-8, 11, 21-26 and 28-33 have been examined. Claims 2-8, 11, 21-26 and 28-33 have been amended. No new matter is added.

Claims 2-8, 11, 21-26 and 28-33 stand rejected under 35 U.S.C. § 112, first paragraph. With respect to claims 2-8 and 11, this rejection has been obviated by the above amendments to claims 2-8 and 11. With respect to claims 21-26 and 28-33, this rejection is obviated in part by the above amendments to the claims and traversed in part for the reasons discussed below.

With respect to claims 21-26 and 28-33, the Office Action states, "It appears from figure 3 that PAO* [para-N-(ethane-2-sulfonic)amino phenylyasrsenoxide] exhibited inhibition of L-selectin shedding" (See Office Action, p. 2). However, this is a misreading of Figure 3. Figure 3 clearly shows that PAO* ***induces L-selectin shedding*** rather than causes " inhibition of L-selectin". That is, after treatment with sufficiently high concentration of PAO*, L-selectin is lost from leukocyte surfaces. The x-axis shows the amount L-selectin that *remains* on the cell surface after the treatment, so a short bar indicates a loss of L-selectin as compared to the untreated ice or 37 deg. controls without the treatment. This shows that PAO* blocks the dithiols that are required for maintenance of L-selectin on the cell surface, so L-selectin is shed. Since HIV requires PDI or other similar dithiols for HIV entry, blockade of all cell surface dithiols is likely to block HIV entry. Also, the Office Action states, " It is not apparent that either of the claimed methods is engendered by the demonstration that one of the claimed compounds inhibits L-selectin shedding" and "[a]ccordingly it is not even clear whether applicants are asserting that compounds which stimulate L-selectin shedding will inhibit viral replication, or whether viral replication is inhibited by compounds which inhibit L-selectin shedding." (See Office Action, p. 3),

once again indicating that claims 21-26 and 28-33 were rejected based on the incorrect idea that the compounds of the present invention inhibit L-selectin shedding. In fact, the compounds of the present invention, such as PAO* (See Fig. 3) and PAO (see page 8, line 20) stimulate L-selectin shedding (See Fig. 3, and page 8, lines 19-25, respectively). Furthermore, because the compounds of the present invention cause L-selectin shedding, the compounds of the present invention will inhibit viral entry, including HIV entry, into a host cell as claimed in claims 28-33. This is true because L-selectin shedding and inhibition of viral entry are caused by the same action of the compounds: blockade of cell surface vicinal dithiols, including the vicinal dithiols required for PDI activity.

For the above reasons, the rejection of claims 21-26 and 28-33 is improper, because the rejection is based on an improper understanding of how the compounds of the present invention may be used as claimed in the methods of claims 21-26 and 28-33, to inhibit PDI and prevent viral infections, respectively.

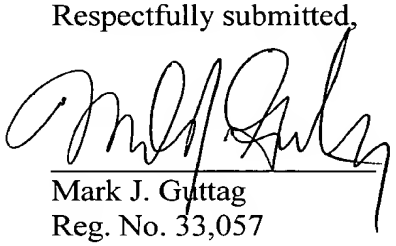
Claims 2-8, 11, 21-26 and 28-33 stand rejected under 35 U.S.C. § 112, second paragraph. The Examiner is thanked for pointing out the specific objectionable language.

Claims 2-8, 11, 21-26 and 28-33 have been amended to comply with the requirements of 35 U.S.C. § 112, second paragraph and to more distinctly define the subject matter of the present invention. In particular, with respect to claims 21-26 and 28-33, claims 21-26 and 28-33 have been amended to include the language suggested by the Examiner on pages 5-6 of the Office Action. For the above reasons, this rejection has been obviated by the above amendments to claims 2-8, 11, 21-26 and 28-33.

If the Examiner has any questions or concerns regarding the present response, the Examiner is invited to contact Mark J. Guttag at 703-591-2664.

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance, and favorable action is respectfully solicited.

Respectfully submitted,



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November 19, 2002

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
ROGELJ *et al.*	)	**Examiner: Lukton, D.**
	)	
Serial Number: 09/424,181	)	
	)	**Art Unit: 1653**
Filed: November 10, 1999	)	
	)	
For: INHIBITION OF CELL SURFACE PROTEIN DISULFIDE ISOMERASE	)	**Docket No.: UNME-0054-1**

Director of the U.S. Patent and Trademark Office
Washington, D.C. 20231

VERSION WITH MARKINGS TO SHOW CHANGES MADE

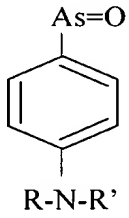
Sir:

Below are the amendments in the accompanying Amendment for the above-identified application shown in redlined format:

IN THE CLAIMS

Please amend the claims, without prejudice or disclaimer, as indicated below:

2. (Twice Amended) A ~~membrane-impermeable inhibitor of protein disulfide isomerase~~compound ~~(PDI)~~ having the formula:



wherein R is either H or a charged ligand containing from 1 to 6 carbon atoms;

wherein R' is either H or a charged ligand containing from 1 to 6 carbon atoms; and

wherein at least one of R and R' is a charged ligand containing from 1 to 6 carbon atoms.

3. (Twice Amended) ~~An inhibitor according to~~The compound of Claim 2,

wherein ~~the at least one of R and R' is a~~ charged ligand containsing at least one SO_3^- group.

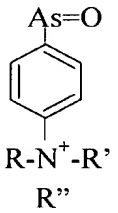
4. (Twice Amended) ~~An inhibitor according to~~The compound of Claim 2, wherein at least one of R and R' ~~the ligand~~ is a straight chain or branched alkyl group containing 1, 3, 4, or 6 carbon atoms and at least one SO_3^- group.

5. (Twice Amended) ~~An inhibitor according to~~The compound of Claim 2, wherein at least one of R and R' ~~the ligand~~ is an aryl group containing at least one SO_3^- group.

6. (Twice Amended) The ~~inhibitor~~ compound of Claim 5, wherein the SO_3^- group is attached to a ring carbon atom.

7. (Amended) The ~~inhibitor~~compound of Claim 6, wherein the SO_3^- group is attached to the ring carbon atom via a C_1 -C_6 -alkylene group.

8. (Twice Amended) A compound ~~membrane-impermeable inhibitor of protein disulfide isomerase (PDI)~~ having the formula:



wherein R is H or alkyl;
wherein R' is H or alkyl;
wherein R" is H or alkyl; and
wherein at least one of R, R' and R" is alkyl.

11. (Twice Amended) The compound of~~An inhibitor according to~~ Claim 2, wherein one of R or R' is ~~an uncharged~~ H ~~or C_1-C_6-alkyl ligand~~.

21. (Amended) A method for inhibiting PDI by exposing cells expressing PDI to a compound according to Claim 2 ~~in an amount sufficient to inhibit PDI activity~~for a time and under conditions effective to inhibit protein disulfide isomerase (PDI).

22. (Amended) A method for inhibiting PDI by exposing cells expressing PDI to a compound according to Claim 3 for a time and under conditions effective to inhibit protein disulfide isomerase (PDI)~~in an amount sufficient to inhibit PDI activity~~.

23. (Amended) A method for inhibiting PDI by exposing cells expressing PDI to a compound according to Claim 4 for a time and under conditions effective to inhibit protein disulfide isomerase (PDI)~~in an amount sufficient to inhibit PDI activity~~.

24. (Amended) A method for inhibiting PDI by exposing cells expressing PDI to a compound according to Claim 5 for a time and under conditions effective to inhibit protein disulfide isomerase (PDI)~~in an amount sufficient to inhibit PDI activity~~.

25. (Amended) A method for inhibiting PDI by exposing cells expressing PDI to a compound according to Claim 6 for a time and under conditions effective to inhibit protein disulfide isomerase (PDI)~~in an amount sufficient to inhibit PDI activity~~.

26. (Amended) A method for inhibiting PDI by exposing cells expressing PDI to a compound according to Claim 7 for a time and under conditions effective to inhibit protein disulfide isomerase (PDI)~~in an amount sufficient to inhibit PDI activity~~.

28. (Amended) A method for treating a mammal for preventing a viral infection propagated by PDI-mediated virion entry into host cells comprising administering to the mammal phenylarsine oxide (PAO) or a compound according to Claim 2 ~~in an amount sufficient~~for a time and under conditions effective to inhibit viral entry into a

host cellpropagation.

29. (Amended) A method for treating a mammal for preventing a viral infection propagated by PDI-mediated virion entry into host cells comprising administering to the mammal phenylarsine oxide (PAO) or a compound according to Claim 3 for a time and under conditions effective in an amount sufficient to inhibit viral entry into a host cellpropagation.

30. (Amended) A method for treating a mammal for preventing a viral infection propagated by PDI-mediated virion entry into host cells comprising administering to the mammal phenylarsine oxide (PAO) or a compound according to Claim 4 for a time and under conditions effectivein an amount sufficient to inhibit viral entry into a host cellpropagation.

31. (Amended) A method for treating a mammal for preventing a viral infection propagated by PDI-mediated virion entry into host cells comprising administering to the mammal phenylarsine oxide (PAO) or a compound according to Claim 5 for a time and under conditions effectivein an amount sufficient to inhibit viral entry into a host cellpropagation.

32. (Amended) A method for treating a mammal for preventing a viral infection propagated by PDI-mediated virion entry into host cells comprising administering to the mammal phenylarsine oxide (PAO) or a compound according to Claim 6 for a time and under conditions effectivein an amount sufficient to inhibit viral entry into a host cellpropagation.

33. (Amended) A method for treating a mammal for preventing a viral infection propagated by PDI-mediated virion entry into host cells comprising administering to the mammal phenylarsine oxide (PAO) or a compound according to Claim 7 in an amount sufficient to inhibit viral entry into a host cellpropagation.